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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,605	09/29/1998	TOM DE VRINGER	98.554	8895
20306 7590 04/16/2007 MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			EXAMINER KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER
			1615	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/16/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/155,605	<b>Applicant(s)</b> DE VRINGER ET AL.	
	<b>Examiner</b> Gollamudi S. Kishore, Ph.D	<b>Art Unit</b> 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-9, 12-17 and 19-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9, 12-17 and 19-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

The response dated 6-12-06 is acknowledged.

Claims included in the prosecution are 1-9, 12-17 and 19-37.

Upon consideration, the 102(e) as being anticipated by Blinkovsky (5,693,516) is withdrawn.

### ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 521 562 of record.

EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol and an active agent. The process of preparation involves making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and claims). Although EP does not explicitly teach that the preparation is in the form of a powder, since it teaches on col. 12, lines 55-56, the removal of the non-polar vehicle (volatile silicon oil), the teachings of a powder form of the preparation are implicit in the reference.

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Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant continues to argue that although DeVringer instructs to remove the non-polar excipients to obtain an instant preparation, DeVringer fails to teach a method for doing so and without a teaching of how to remove the non-polar vehicle, the ordinary artisan could not arrive at the presently claimed powder of reversed vesicles. This argument is not persuasive. The removal of organic solvents is well known in the art and especially it is within the skill of the art to realize that the silicon oil is volatile and therefore, it could be removed easily. If there were no method existing in the art for the removal of an organic solvent or non-polar excipients, DeVringer would not have instructed (applicant himself recognizes that DeVringer instructs the removal).

Therefore, applicant's arguments that

the Office has not provided evidence or scientifically based reasoning that as of the time of filing the present invention one of ordinary skill in the art would have necessarily known of and employed a method of removing non-polar vehicles that would necessarily lead not merely to a powder, but to a powder of reversed vesicles having the properties recited in the present claims are not persuasive. Applicant's arguments that not every method of removing the non-polar vehicle from the various dispersions of DeVringer will result in a powder as presently claimed are not persuasive since it is not accompanied by experimental evidence. Furthermore, according to instant specification on page 5, lines 14-25, the removal of apolar vehicle is done by either rotational evaporation or by spray drying; DeVringer teaches rotational evaporation method. In addition, as pointed out before, DeVringer teaches reversed vesicles in a non-polar

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medium and on col. 12, lines 46-56 clearly states, "After having obtained a dispersion of vesicles according to one of the above-mentioned method, additional production steps comprise:

- reducing the size of the vesicles by methods known in the art (sonication, extrusion, micro fluidization)
- polymerizing the vesicles in case a polymerizable surfactant is used by methods known in the art;
- ***removing the non-polar excipient(s) to obtain an instant preparation***".

This last statement in the prior art clearly implies that that the non-polar excipient is removed contrary to applicant's arguments that conventional techniques for removing the vehicles cannot be applied to reversed vesicular systems without undue experimentation.

With regard to applicant's arguments that the office has not provided evidence or scientifically based reasoning that as of the time of filing the present invention one of ordinary skill in the art would have necessarily known of and employed a method of removing non-polar vehicles that would necessarily lead not merely a powder, but to a powder of reversed vesicles having the properties recited in the present claims, the examiner points out that preparation of liposomal powders (reverse vesicles) which could be reconstituted into liposomes again upon the addition of a medium is known in the art as the prior art applied below.

*Claim Rejections - 35 U.S.C. § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0521562 by itself or in further combination with EP 0 678 295, EP 0159237, GB 2002319, JP 05194253 by themselves or in combination (all are of record).

According to instant claims, the preparation is a reversed vesicle, meaning that the hydrophobic group of the surfactant molecule is oriented toward the hydrophobic continuous medium, which is an oil (silicone oil).

As pointed out above, EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol, a hydrophilic stabilizing factor, and an active agent. The process of preparation involves

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making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and claims). What this reference lacks are the explicit teachings that the preparation is in the powder form.

EP 0678 295 teaches that vesicular preparations (hydrophilic group of the lipid is oriented towards the continuous external phase (water) can be lyophilized to form powders (note Example 1 and claims 1 and 7).

EP 0159237 teaches that emulsions (micelles) can be freeze-dried to form powders, which are easier to handle than emulsions (note the abstract).

GB teaches that dehydration of lipid vesicles (liposomes) to prepare a stable powder, which can be stored for longer periods of time (note the abstract).

JP 05194253 teaches the preparation of a powder of reverse micelles containing a surfactant (note the abstract).

Assuming that the preparations taught by EP 0521 562 are not powder preparations, it is deemed obvious to one of ordinary skill in the art that if the removal of the external medium in which the vesicles are dispersed results in a powdery preparation as evidenced by the references of the references of EP 295, EP 237 and JP 253. One of ordinary skill in the art would be motivated to remove the external medium such as volatile silicone oil and prepare the powders since GB teaches that powders are stable and can be stored for longer periods of time.

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Applicant's arguments have been fully considered, but are not persuasive. The examiner has already addressed applicant's arguments with regard to EP. Applicant further argues that none of the references relate to the removal of a non-polar from a reversed vesicle and therefore, one of ordinary skill in the art would not be motivated to combine the teachings of such art with EP 562. The examiner disagrees. The references show the state of the art in the preparations micelles, emulsions, liposomes and even reverse micelles in powder form. With regard to JP, applicant argues that the abstract mentions nothing about powder. The examiner points out that line 3 of the abstract recites reverse 'micelles' and lines 4 and 5 recite 'reverse micelle powder'. With regard to applicant's arguments that the present claims are not merely directed to a powder of reversed vesicles, rather they are directed to a powder of reverse vesicles that, when suspended in a biodegradable oil, yield a higher percentage of reverse vesicles than (sic, than) when the same amount of reversed vesicles is prepared directly in the biodegradable oil, the examiner points out that this is an intended function and applicant has not shown that EP reverse micelles do not function the same way. In essence, EP 562 teaches reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is volatile silicone oil and the removal of oil. Instant claims do not differentiate from the prior art product. The examiner disagrees with applicant that the references cited are non-analogous art since they deal with the state of the art of preparing encapsulated drug powder preparations including liposomes, which are reverse vesicles.



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5. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0521562 in combination with Blinkovsky cited above.

As pointed out above, EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol, a hydrophilic stabilizing factor, and an active agent. The process of preparation involves making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and claims). What this reference lacks are the explicit teachings that the preparation is in the powder form.

Blinkovsky discloses dried preparations of reverse micelles containing surfactants (abstract, col. 1, line 66 through col. 3, line 53, examples and claims).

It would have been obvious to one of ordinary skill in the art to remove the solvent and prepare the composition of EP in a powder form with a reasonable expectation of success since Blinkovsky teaches that dried preparations of reverse micelles can be made by evaporating the external medium.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that DeVringer is concerned with the production of dispersions of vesicles while Blinkovsky is concerned with the preparation of dispersions and compositions containing micelles. Therefore, one skilled in the art would not have considered combining the teachings of DeVringer with Blinkovsky

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because they are concerned with fundamentally different problems and are, therefore, non-analogous art. This argument is not persuasive since Blinkovsky is concerned with **reverse** micelles and not just micelles and because the evaporation method used in both is the same, that is, rotoevaporation (col. 6, lines 19-23).

**6. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Gollamudi S Kishore, Ph.D  
Primary Examiner  
Art Unit 1615

Gsk